Estrogen augments the vasodilatory effects of vascular endothelial growth factor in the uterine circulation of the rat.

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OBJECTIVE: Pregnancy augments uterine artery vasodilatation in response to vascular endothelial growth factor, although the underlying mechanism is not known. The aim of this study was to test the hypothesis that estrogen and progesterone, the primary sex steroids of pregnancy, are responsible for this effect through increased endothelial secretion of nitric oxide. STUDY DESIGN: Adult female Sprague-Dawley rats underwent oophorectomy at 9 weeks of age with concomitant placement of 21-day timed-release pellets containing either 17beta-estradiol (n = 6) or progesterone (n = 6), or a combination of these (n = 6). Control rats also underwent oophorectomy but did not receive hormone replacement (n = 6). Two to 3 weeks after oophorectomy the rats were killed and the main uterine artery was dissected free, cannulated in an arteriograph, and pressurized to 50 mm Hg. After constriction with phenylephrine, concentration-response curves to vascular endothelial growth factor (0.1-20 nmol/L) were performed to compare arterial sensitivity to and maximal effects of vascular endothelial growth factor among the 4 treatment groups. Vessels were then treated with N omega-nitro-L -arginine (0.24 mmol/L), an inhibitor of nitric oxide synthase, and the maximally effective concentration of vascular endothelial growth factor was reapplied to evaluate the relative contribution of nitric oxide to the overall effect. RESULTS: Comparisons of the effective concentration of vascular endothelial growth factor that elicited 50% of the

maximal dilatation revealed the vessels of the estrogen group to be approximately 10 times more sensitive than the control group (0.4 +/- 0.11 nmol/L vs 4.2 +/- 1.13 nmol/L, respectively; P < . 05). Responses of vessels from the progesterone and combined groups were intermediate (progesterone, 2.3 +/- 0.66 nmol/L; combined, 1.1 +/- 0.28 nmol/L). Maximal vasodilatory responses were greatest in the groups with treatment including estrogen (estrogen, 61% +/- 3. 1%; combined, 54% +/- 3.4%; progesterone, 42% +/- 5.8%, control, 40% +/- 3.5%; P < .05). Addition of N omega-nitro-L -arginine inhibited maximal vascular endothelial growth factor-induced dilatation by approximately 40% irrespective of treatment group. CONCLUSION: The presence of estrogen rather than progesterone leads to an enhancement of vascular endothelial growth factor-induced arterial dilatation during pregnancy. This effect results from a proportional increase in endothelial nitric oxide secretion, along with that of another, as yet unidentified vasodilatory substance.

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